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09/578,849	05/26/2000	Michael Z. Martin	031727.0001A	7983

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EXAMINER

PRATS, FRANCISCO CHANDLER

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 03/31/2003

21

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/578,849

Applicant(s)

MARTIN ET AL.

Examiner

Francisco C Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 13 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 99-121 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 99-121 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 13, 2003, has been entered.

The amendment filed January 13, 2003, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 17-19 and 79-98 have been cancelled.

Claims 99-121 have been added.

Claims 99-121 are pending and are examined on the merits.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 99-121 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point

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out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "high pressure" in claims 99 and 116 is indefinite because it is not clear how high the pressure must be. Because the claim fails to clearly delineate between the claim-encompassed subject matter and the non-claim-encompassed subject matter, a holding of indefiniteness over claims 99 and 116 and their dependents is clearly required.

Similarly, the recitation "high recovery" in claims 105 and 110 renders those claims and their dependents indefinite, because it is not clear what amount of recovery is required by the claims.

The recitation "p. 32, line 11, Table 1]" in claim 110 appears to be a typographical error. Its presence in that claim renders it confusing, and therefore indefinite.

Claim 114 is indefinite in that it is not clear what "analysis time" is being referred to. Claim 114 depends from claim 110, and that claim does not recite any analysis step. Moreover, it is not clear actual process steps are required by the "using" step in claim 114, since the claim appears to be entirely unrelated to the previous claim.

Claim 117 is indefinite because it states that the supercritical fluid "is" CO<sub>2</sub> and alcohol, yet the previous claim

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requires the fluid to contain CO<sub>2</sub> and alcohol and isopropylamine.

Claim 117 therefore does not properly depend from claim 116.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 120 and 121 are rejected under 35 U.S.C. 102(b) as being anticipated by Lopez-Avila et al (J. High Resol. Chromatogr. 20:555-559 (1997)).

Because claims 120 and 121 recite products made by a method "comprising" certain steps, claims 120-121 encompass products made by processes which include steps resulting in compounds purified to homogeneity. Thus claims 120 and 121 encompass purified kava lactones such as those whose structures are disclosed by Lopez-Avila. A holding of anticipation is clearly required.

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***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 99, 102-104 and 116-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castor (U.S. Pat. 5,750,709) in view of Berger et al (J. Pharmaceutical Sciences. 83(3):281-286 (1994)).

Castor discloses a process comprising two supercritical extraction steps, wherein the second step is a chromatographic step, as recited in the claims. See column 4, lines 39-61. Note specifically that the term "resin trap" in applicant's claims encompasses any chromatographic material, including that

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used by Castor. Note Castor's use of the claimed solvents, including ethanol column 5, lines 54-62. Note further that Castor '709 discloses that the techniques disclosed therein are applicable generally to virtually any biomass which potentially contains therapeutic materials, including alkaloid compounds such as vincristine and vinblastine. See Castor '709 at col. 4, lines 35-38, see also claim 14 at column 33. Disclosed advantages of the technique include improved production capacity, improved scalability, greater overall efficiency, fewer processing steps, and improved product quality. See Castor '709 at col. 7, lines 23-37.

Castor differs from the claims in failing to disclose the use of isopropylamine in the supercritical extraction processes disclosed therein. However, Berger clearly discloses that, in supercritical extraction processes using carbon dioxide and ethanol, isopropylamine is extremely useful in the resolution of compounds which contain the same heterocyclic amine moieties as the alkaloids disclosed in Castor. See page 281, abstract. In fact, Berger discloses that without isopropylamine present "none of the solutes eluted." Abstract.

Thus, the artisan of ordinary skill at the time of applicant's invention, motivated by Castor to purify heterocyclic amine containing alkaloid compounds from plant

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materials using supercritical fluids containing carbon dioxide and alcohol, clearly would have been further motivated by the excellent results of Berger to have included isopropylamine in the extractant fluids to have ensured and/or improved the resolution of the heterocyclic amine containing compounds recovered from the plant material. A holding of obviousness is therefore required.

Claims 99 and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castor (U.S. Pat. 5,750,709) in view of Berger et al (J. Pharmaceutical Sciences. 83(3):281-286 (1994)), and in further view of Bejar et al (Int. J. Pharmacognosy 33(1):25-32 (1995)).

As discussed above, Castor and Berger clearly suggest including isopropylamine in the fluids used to purify compounds from plants by supercritical fluids. Neither Castor nor Berger discloses the use of such a process when extracting compounds from *Byrsonima crassifolia*. However, Bejar clearly discloses that *Byrsonima* contains a number of amine containing compounds, including heterocyclic amines, such as pipecolic acid. Thus, the artisan of ordinary skill, using supercritical fluids to extract *Byrsonima* so as to afford the advantages disclosed by Castor, clearly would have been further motivated by Berger to



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have included isopropylamine in the supercritical solvent so as to ensure/improve resolution of the heterocyclic amine containing compounds known to be present in *Byrsonima*. Absent some unexpected result, a holding of obviousness is clearly required.

Claims 105-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lopez-Avila et al (J. High Resol. Chromatogr. 20:555-559 (1997)) and Schwabe (U.S. Pat. 5,296,224) in view of Castor (U.S. Pat. 5,440,055) and Castor (U.S. Pat. 5,750,709).

Each of Lopez-Avila and Schwabe disclose the preparation of extracts of kava root containing specific pharmacologically useful compounds, including kava lactones. See Lopez-Avila at abstract; see Schwabe '224 Examples 1-4, at cols. 3-7. Although the extraction performed in Lopez-Avila is conducted under supercritical conditions, Lopez-Avila and Schwabe differ from the claims in that neither reference uses supercritical, critical or near-critical conditions during the chromatography step for extraction of the pharmacologically useful compounds.

However, both Castor '055 and '709 disclose that supercritical, critical or near-critical chromatography, using the claimed solvents including ethanol, is a useful technique in recovering therapeutic compositions, such as taxols, from

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natural materials. See, e.g., Castor '709 at abstract.

Disclosed advantages of the technique include improved production capacity, improved scalability, greater overall efficiency, fewer processing steps, and improved product quality. See Castor '709 at col. 7, lines 23-37. Note specifically that Castor '709 discloses that the techniques disclosed therein are applicable generally to virtually any biomass which potentially contains therapeutic materials. See Castor '709 at col. 4, lines 35-38.

Thus, the artisan of ordinary skill at the time of applicant's invention, seeking to prepare therapeutic compositions from kava root according to Lopez-Avila or Schwabe, would have been motivated by the Castor patents' disclosure of the advantages of supercritical, critical or near-critical chromatography to have employed supercritical, critical or near-critical chromatography to obtain therapeutic compositions and/or compounds from kava root. A holding of obviousness is therefore required.

It is noted that none of the cited references discloses the specific column media recited in claim 110, or the temperatures and pressures recited in other claims. However, the claimed chromatographic column media were well known in the art at the time of applicant's invention. Thus, the artisan of ordinary

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skill would clearly have considered the determination of a suitable column media for chromatographic purification of a particular compound or compounds to be a matter of selecting from among known equivalents recognized in the art to be useful in the processes disclosed in the Castor patents.

Moreover, the artisan of ordinary skill would have recognized that the determination of suitable temperatures and pressures for running Castor's columns, as recited in the claims, would have been a routine matter of optimization on the part of the artisan of ordinary skill, and therefore necessarily *prima facie* obvious under § 103(a). In this regard, note specifically that applicant's claims recite extracting the kava lactones under conditions which Lopez-Avila discloses are suitable for solubilizing those compounds. See Lopez-Avila at page 555, paragraph entitled "2.1 Supercritical Fluid Extraction (SFE)", discussing the extraction of kava lactones in carbon dioxide containing 15% ethanol, at temperatures of 60 degrees, and pressures ranging from 250 atm to 450 atm. Thus, applicant's claims recite extractions under conditions known to render the claimed compounds soluble. Absent some evidence of an unexpected result inhering from the use of a particular chromatographic column medium, or particular temperatures or pressures, the determination of suitable chromatographic

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conditions for application to Castor's techniques must therefore be held as obvious.

### ***Response to Arguments***

All of applicant's argument has been fully considered but is not persuasive of error. With respect to those embodiments within claims 105-115 which allegedly encompass unexpected results, applicant has not provided any explanation of the data in the specification, nor is it clear that the extractions performed in the specification have been compared to the prior art. Simply put, applicant has not argued or demonstrated *why* the claimed embodiments demonstrate an unexpected result over the prior art, or for that matter, which claimed embodiments are considered to contain unexpected results. Thus, applicant clearly has not met their burden of demonstrating any unexpected result vis-à-vis the prior art, particularly the Lopez-Avila reference. Further still, the fact that the prior art uses multiple extraction steps and/or solvents does not demonstrate non-obviousness, in view of the fact that the open language of the claims encompasses exactly such processes. In short, the claims do not exclude such processes. The claims therefore are not different from the prior art in this respect.

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No claims are allowed. However, claims 100 and 119 are considered free of the prior art and would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims. Specifically, as discussed above, isopropylamine is disclosed in the prior art as significantly improving the resolution in supercritical fluid extraction of nitrogen-containing heterocyclic compounds from mixtures containing those compounds. In view of the fact that the pharmacologically active compounds of kava, the lactones, do not contain such nitrogen-containing moieties (see Lopez-Avila, page 555), the artisan of ordinary skill would not have been motivated to have applied isopropylamine to the supercritical fluid extraction processes of kava root disclosed in the prior art.

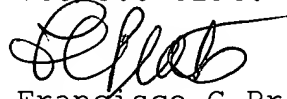
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can

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be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Francisco C Prats  
Primary Examiner  
Art Unit 1651

FCP  
March 27, 2003